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Short Communication

Chimerism 47,XY,+21/46,XX in a female infant with anencephaly and other congenital defects

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Abstract

Chimerism is rare in humans and is usually discovered accidentally when a 46,XX and 46,XY karyotype is found in a same individual. We describe a malformed female infant with neural tube defect (NTD) and a 47,XY,+21[5]/46,XX[30] karyotype.

Key words: chimerism, anencephaly, trisomy 21.

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Chimerism is rare in humans and has been classified into two categories. Partial chimerism can be found in dizygotic twins, foeto-maternal transplacental exchange or graft due to blood interchange. The other type is constitutional or whole-body dispermic chimeras, which are the result of the fusion of two or more different zygotes into a single new body (Ford, 1969). Constitutional chimerism is usually detected in individuals with at least two different lineages with regard to sex chromosome complement. Several patients have been reported with 46,XX/46,XY karyotypes and ambiguous genitalia (Fitzgerald *et al*, 1979; Giltay *et al*, 1998). Chimerism has also been reported in cases in which a normal lineage coexists with an abnormal one, each carrying a distinct sex chromosome complement (Sawai *et al*, 1994; Wiley *et al*, 2002).

Here, we describe a case of 47,XY,+21[5]/46,XX[30] chimerism in a foetus with anencephaly and other associated malformations. This case has been included in a large study previously approved by the ethics committee of our institution and informed consent was obtained from the parents.

The proposita, a female infant, was born weighing 1,060 g of young and nonconsanguineous parents after 33 weeks of a twin gestation. Prenatal ultrasonography at 9 weeks showed a twin gestation with a monochorionic diamniotic placenta. At the end of the second trimester, another ultrasound examination demonstrated acrania, vertebral malformations, pulmonary hypoplasia, dextrocardia and a possible diaphragmatic hernia in one foetus. Delivery was normal. The first twin, a female preterm infant, weighed 1,905 g and was clinically normal. Her karyotype from peripheral lymphocytes was 46,XX in all 50 analyzed metaphases. The proposita died one hour after birth. She had anencephaly, cervical rachischisis, discrete retroflexion of the head, absence of neck, submucous cleft palate, trunk-limb disproportion, thoracic scoliosis, rigidity at elbows, camptodactyly with clinodactyly of fifth fingers and prominent calcaneous. X-ray examinations showed: complete absence of the calvaria, cervical rachischisis, hemivertebrae of T8 and T12, cervico-thoracic scoliosis, 11 ribs on the right and 9 on the left with fusion of some ribs on the left (Figure 1). Necropsy revealed absence of left kidney, a mesenteric fold at the transverse colon and uterus unicornis.

The karyotype of lymphocyte metaphases from cardiac blood was 47,XY,+21[5]/46,XX[30]. Interphase-FISH studies using 13/21 satellite probe D13Z1/D21Z1 (Qbiogene, USA) showed 5 green signals in 3 out of 1,500 nuclei analyzed. In simultaneous hybridization with X and Y α-satellite probes (DXZ1, DYZ1, Cytocell, UK) 3 out of 1,500 nuclei showed one signal of each probe. The remainder nuclei presented only two green signals of the X chromosome probe. The discrepancy between the frequency of trisomic cells that we observed in metaphases (14%) and in interphase nuclei using FISH (0,2%) is intriguing. It could be due to sample error, considering the small number of metaphases analyzed. It is noteworthy that the frequency of XY interphase was the same as the frequency of trisomic cells, in separate FISH experiments. Therefore it seams that the proportion of trisomic XY cells in the infant was very small, as demonstrated by FISH.

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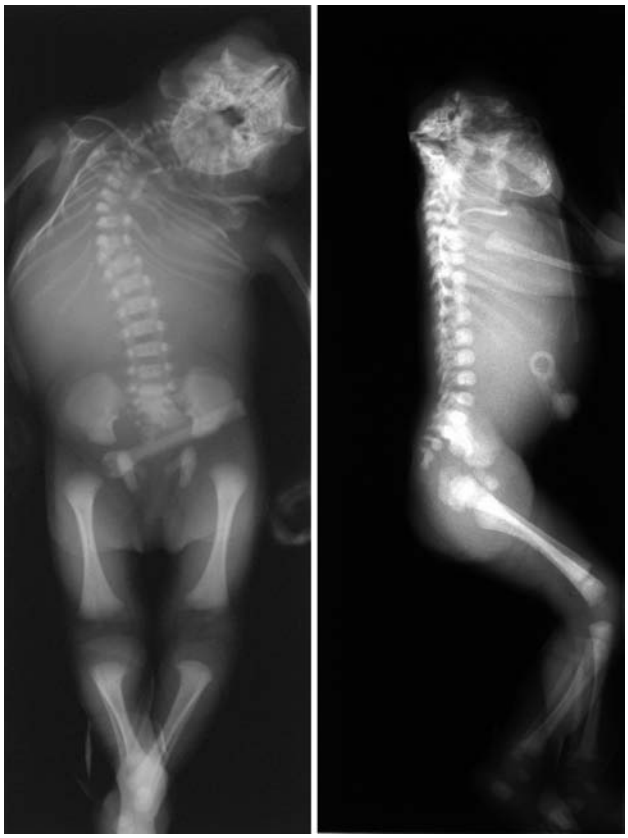

Figure 1 - Partial babygram of the foetus. Note absence of the calvaria and vertebral defects.

The case presented here was a multiple malformed infant with craniorachischisis, vertebral defects, urogenital malformations, and chimerism 47,XY,+21/46,XX. A similar type of chimerism was reported by Sawai *et al* (1994) in an infant with no manifest Down syndrome, but having ambiguous genitalia. These authors reported a frequency of the trisomic line of 2% in lymphocytes and 4% in fibroblasts. In the infant examined by us the predominance of 46,XX cells in the genital ridges seems to be the best explanation for the absence of virilization.

The association of trisomy 21 and anencephaly has been referred as "occasional" by Schinzel (1983). In a recent large study of major malformations in 5,581 cases of Down syndrome, spina bifida was the only neural tube defect found (Källén *et al*, 1996). Unpublished data from our Perinatal Genetics Programme also failed to show this association in 153 cases presenting anencephaly/craniorachischisis nor was there any association with 146 neural tube defects consisting of spina bifida and encephalocele.

Fusion of two zygotes is the main mechanism put forward to account for chimerism and we suggest that for the case described in this paper two zygotes, one 46,XX and the other 47,XY,+21, were initially formed, the 46,XX zygote giving two identical embryos and fusion between one of these twins and the 47,XY,+21 zygote producing the chimera.

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